

**CLAIMS**

1. A method of inhibiting NF- $\kappa$ B induction in a cell comprising administering an effective amount of a peptide which blocks the interaction of one or more IKKs and NEMO.

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2. The method of claim 1 wherein the IKK is selected from the group consisting of IKK $\alpha$  and IKK $\beta$ .

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3. The method of claim 1 wherein the peptide comprises at least one NEMO binding domain.

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4. The method of claim 3 wherein the peptide further comprises at least one membrane translocation domain.

5. The method of claim 3 wherein the NEMO binding domain is selected from the group consisting of SEQ ID NO: 2, 4, 5, 6, 11, 12, 16 and 17.

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6. A method of inhibiting inflammation in a mammal comprising administering an effective amount of a peptide which blocks the interaction of IKK and NEMO.

7. The method of claim 6 wherein the peptide blocks the recruitment of leukocytes into sites of acute and chronic inflammation.

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8. The method of claim 6 wherein the peptide down-regulates the expression of E-selectin on endothelial cells.

9. The method of claim 6 wherein the peptide blocks osteoclast differentiation.

10. A method of inhibiting NF- $\kappa$ B-dependent target gene expression in a cell comprising administering an effective amount of a peptide which blocks the interaction of one or more IKKs and NEMO.

5 11. The method of claim 10 wherein the IKK is IKK $\beta$ .

12. The method of claim 10 wherein the NF- $\kappa$ B-dependent target gene is E-selectin.

10 13. A method of identifying an agent which interacts with the NEMO binding domain comprising the steps of:

(a) exposing cells which express NEMO and NF- $\kappa$ B to an agent; and  
(b) determining whether the agent modulates activation of NF- $\kappa$ B by the cell, wherein an alteration in activation of NF- $\kappa$ B is indicative of an agent which interacts with the NEMO binding domain.

15 14. A method of identifying an agent which modulates the activity of NEMO comprising the steps of:

(a) exposing cells which express NEMO to an agent; and  
(b) determining whether the agent modulates the activity of NEMO, thereby identifying an agent which modulates the activity of NEMO.

20 15. A fusion peptide comprising the NEMO binding domain and at least one membrane translocation domain.

25 16. The fusion peptide of claim 15 wherein the membrane translocation domain facilitates membrane translocation *in vivo*.

17. The fusion peptide of claim 15 wherein the membrane translocation domain is selected from the group consisting of the third helix of the *antennapedia* homeodomain and HIV-1 Tat protein.

5 18. The fusion peptide of claim 15 wherein the NEMO binding domain is selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 and 17.

19. An isolated peptide selected from the group consisting of:  
(a) an isolated peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 and 17, 18 and 19;

15 (b) an isolated peptide comprising a fragment of at least three amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19;  
(c) an isolated peptide comprising conservative amino acid substitutions of the amino acid sequences selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19;

20 (d) naturally occurring amino acid sequence variants of amino acid sequences selected from the group consisting of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19.

20. A composition comprising the peptide of claim 15 or 19.

25 21. The composition of claim 20 further comprising a carrier.

22. An isolated peptide consisting of the amino acid sequence of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19.

23. An isolated nucleic acid molecule selected from the group consisting of: (a) an isolated nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19, and (b) an isolated nucleic acid molecule that encodes a fragment of at least three (3) amino acids of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19.

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